Pedersen M, Feddersen D, Pedersen J, Rajan S (2008). Diagnostics related to traditional treatment of medical laryngolical disorders. *International conference on advances in laryngeal biophysiology, Madison Wisconin (by invitation).*

Diagnostics related to traditional treatment of medical laryngological disorders.

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- Usually medical treatments of laryngological disorders are not considered **evidence based** related to clinical trials.
- In the future
- 1. **allergies** diagnosed by medical history and tests of inhalation allergens, other allergies and food additives should have reference to more basic function tests as it is the case with genetic intolerance to cow milk.
- 2. **infections** should be diagnosed with swabs and blood examinations but also be related to cellular physiology.
- 3. **reflux** patients diagnosed with oesophagoscopy and gastroscopy should be examined for basic cellular physiological connections.
- In the future
- **Treatment therefore would be much more systematic and structured than now a days**.
- The aspects include the biomechanical effect of steroids inhalers (without lactose), anti- histamines, antibiotics, acid pump inhibitors, environment corrections including diet and others.

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Introduction

- Aim: To show the necessity of treatments of the inflammatory disorders of the larynx.
- There is a lack of scientific documentation of laryngeal disorders.
- Voice therapy or surgery have been the only accepted scientific possibilities for non-malignant and non-neurological disorders of the larynx.

- Earlier historical **interpretations of upper airway mucosa disorders** are presented, and research aspects for the future commented.

- Based on our 2 earlier Cochrane reviews showing NO evidence of any treatment for vocal nodules or laryngeal pharyngeal reflux, also due to a lack of evidence based measurement:
- three studies were carried out on updated treatment of mucosal pathology, and will be presented.
- These studies highlight the clinical voice related documentation in an evidence based way (a study will soon be finished specifying mucosal treatments)

- Too little attention and focus of research is given to the relevance and importance of **the larynx and voice as a part of the upper airways.**

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historical interpretations of upper airway mucosa – clinical aspects

- Evaluation of primary and secondary immunological deficiencies before tonsillectomy must also be taken into account (Burton et al.)
- Treatment of acute otitis media and indications for tubulations of the drums are under discussion. No evidence was found of tubulations (Lous et al.).
- Inhaled allergens as a reason only for allergic inflammation of the nose (Fokkers et al).
- The lack of relationship to food cannot be extrapolated to the throat where the respiration- voice- and swallowing processes are combined.
- The *historic diagnosis of functional disorder cannot be used as a basis for a review of treatments, neither for ears- noses- nor throat disorders, because the diseases have not been medically defined. Diagnoses must be well defined* and updated, also taking mediators of inflammation of the larynx into account.

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- .

- **As for the clinical aspects of inflammation of the larynx, both the diagnoses and the treatments in randomised controlled trials and reviews till now were non-existent. The model for clinical trials,**
- **though, still seems to be optimal (Pocock)**

Newer mucosal aspects of larynx inflammatory disorders

- Too little focus has been made on the perspective of steroid receptors and neurotransmitters.
- Pharyngitis and laryngitis treatment with new antibiotics that concentrate in pathological mucosa needs more attention.
-
- *lack of respect for good clinical diagnostics of the larynx and evidence based treatments*
- Anti-inflammatory strategies are necessary for the larynx
- For pharyngitis, novel defence mechanisms by streptococcus pyogenes have been detected
- The cough reflex is related to nasal histamine function.Neurogene systems of the upper airways have, till now, little clinical implementation. Primary and secondary immune deficiencies must be taken into account.

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- The defence mechanisms of the upper airways (also relevant for the larynx) are e.g. epitheliac cells, mast cells and leucotrienes
- Exposures of e.g. air condition - to the nose and lungs elicit
- early and late phase allergic inflammatory reactions for the upper and lower airways.
- No conclusion can be made of allergen provocation on voice quality.

- The relation between lower respiratory tract infection caused by respiratory syncytial virus and immune–mediated disease seems to be related to virus provocation of allergy. Histamine in food has been shown to provoke immediate as well as delayed symptoms of 50% of females, and can be used for testing
- The nitric oxide in the upper airways documents treatment effect. .

- It has become more and more clear that a single target approach is unlikely to be effective for the treatment of inflammatory upper airway disease. Detailed understanding of the cellular components and interaction in the inflammatory network of the airway system may lead to better rational targeting of multiple cells and mediators in the treatment of airway inflammation.

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Review of three studies

- 1
- Pedersen M, Beranova A, Møller S. (2004) Dysphonia: **Medical treatment versus a medical voice hygiene advice approach**. European Archives of Otorhinolaryngology 261; 6:312-315
- 2
- Pedersen M, Yousaf U. (2006) **Videostroboscopic expert evaluation of the larynx with running objective voice measurement at the same time gives more secure results than videos alone**. Japan. The 5th International Conference on Voice Physiology and Biomechanics: 110-113 (by invitation).
- 3
- Pedersen M, Munck, K (2007) **A prospective case-control study of normals versus pathological laryngeal cases - and a cohort study for treatment of jitter%, shimmer% and Qx%, glottis closure, cohesion factor (Laryngograph Ltd.) and Long Time Average Spectra,** Cost 2103, MAVEBA Italy: 61-64.

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Study 1

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Pedersen M, Beranova A, Møller S. (2004) Dysphonia: Medical treatment versus a medical voice hygiene advice approach. European Archives of Otorhinolaryngology 261; 6:312-315

- Aim:"role of the medical approach in the treatment of dysphonic patients, in the literature referred to as having non-organic benign vocal fold disorders".
- Comparison of medical treatment of mucosal disorders versus voice hygiene instruction was carried out by one experienced laryngologist for 5-10 minutes (MP).

Materials

- 30 consecutive prospectively randomized Danish-speaking patients (non musical professionals)
- Persistent dysphonia without vocal cord abnormalities
- Medical voice advice (voice training) OR with an updated medical pharmacological diagnosis and therapy.
- Exclusion criteria: organic voice disorder of polyps, papilloma, tumour or paralysis of the vocal cords were found, pregnancy, the patient was under the age of 18, malignancy, neurological or psychiatric disorders.
- The mean ages in the groups were:
- 38.9 years in the medical group.
- 40.7 years in the voice-hygiene group.
- 48.9 years in the retrospective group.
- The duration of the treatment was one month.

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Methods

- General Ear-Nose-Throat examinations and objective analysis
- Videostroboscopy
- Quality-of-life questionnaire (with mean scores for the social, emotional domain, physical functioning domain and overall voice quality).
- Phonetograms with averaging were made for each patient with DPA miniature microphone at 30 cm distance from the mouth.
- **Figure 1** (following slide) show examples of a phonetographic analysis.
- Measurements were repeated after one month, and hereafter analysed with standard deviations.
- A comparison was made between the traditional updated medical treatment group of upper airway mucosa vs. those individuals receiving only medical voice advice (based on cowork with Kirsten Thyme for many years)

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Figure 1

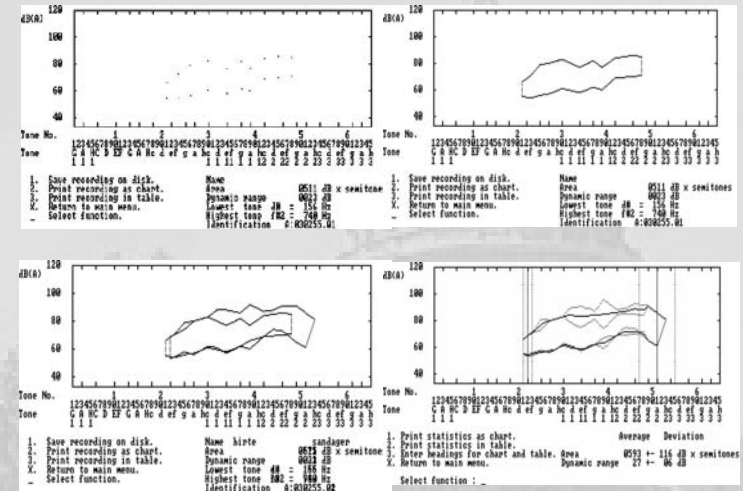

Figure 1:
The co-ordinate system have the notes of a European C-major scale (c-d-e-f-g-a-c) on the x-axis, and dB(A) on the y-axis sung a note, a dot will emerge in the co-ordinate system at the point of the note sung at the right amount of decibel. Upon completion, the computer produces lines between the dots and a model emerges on the computer screen. This model displays the range of the patient's voice. Refer to footnote 1 for procedural information.
The figures to the left show:
- The emerged dots (top left corner)
- The model (top right corner)
- A comparison of models (bottom left corner)
- A further comparison of models with standard deviations (bottom right corner).

- [1] PROCEDURE: Phonetograms are audiograms of the voice. The purpose of the examination is to chart the patient's extent of voice: How loud or soft the patient can reproduce the note and the pitch. A DPA dynamic microphone is held at a distance of 30 cm from the patient's mouth. The patient imitates a note generated by the machine in one semitone area, first as loud as possible, followed by as soft as possible. The patient sings (upwards and downwards) until the patient's limit is reached. A co-ordinate system, where the notes of a European C-major scale, is along the x-axis, and decibels up the y-axis, records a dot for each note sung by the patient. At completion of the procedure, the computer produces connecting lines between the dots, representing the notes. The resulting model clearly shows the range of a patient's voice. This is demonstrated in **figure 1** (the dots, and then the resulting model).

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Results

- At the end of the period, the all subjective opinions of the patients were that 'they felt better', regardless of which group they had been assigned to.
- **Table 1** shows the Voice-related quality of life questionnaire, results of the randomised prospective pilot study of the new patients with follow-up after 1 month quality of life.

Mean score	Medical treatment group N 9	Before	After	Difference	Medical voice-hygiene advice group N 7	Before	After	Difference
Social emotional domain		74.3	87.5	13.2		69.6	76.8	7.1
Physical functioning domain		63.9	84.7	20.8		64.9	73.8	8.9
Overall voice related quality of life		68.1	85.8	17.8		66.8	75.0	8.2

Table 1: Voice-related quality of life questionnaire, results of the randomised prospective pilot study of the new patients with follow-up after 1 month

- The non linear McNemar test for videostroboscopy: no changes of slight abnormalities of the vocal cords.
- An effect was found on the voice-related quality-of-life score test (all three parameters) after medical treatment as well as after medical voice-hygiene advice (mean score difference was 17.3 vs. 8.0).
- Phonetograms; larger range after the one-month treatment period than before the treatment for the group that was treated medically. The maximum dynamic range changed from 18.7 to 22.8 dB.
- The mean phonetogram area in dB times semitones also improved significantly (with a change from 257.7 to 380.9). The medical voice-hygiene advice group also showed improvement of the maximum dynamic range, although smaller (improved with 2.4 dB). The phonetogram area improved with 135.5 dB times semitones.
- In the group that was previously treated medically and that came in for supplementary medical treatment:
- Improvement of the mean dynamic range of 2.9 dB;
- the mean improvement of the phonetogram area was 86.4 dB times semitones.
- No statistical difference between the group treated medically and the one with medical hygiene therapy was found.
- All patients improved by objective analysis.
- **Based on the results, it is suggested that a combined approach of medical treatment and medical voice hygiene advice may be used in the future and analysed in prospective randomised controlled studies.**

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Study 2

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Pedersen M, Yousaf U. (2006) Videostroboscopic expert evaluation of the larynx with running objective voice measurement at the same time gives more secure results than videos alone. Japan. The 5th International Conference on Voice Physiology and Biomechanics: 110-113 (by invitation).

- Aim: to obtain "a statistical significant evidence of the videostroboscopic picture made in combination with voice analysis".
- This study is part one of two: a prospective case-control study and a cohort study of treatment.

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- **Materials**
- All patients coming in with complaints of a laryngeal disorder with hoarseness and a lump in the throat were analysed in a period of 4 months.
- 378 clients were included in this study, in which 35 were without voice complaints, and 338 patients were with dysphonia, diagnosed for medical aspects in the larynx and upper airways.
- The 35 consecutive patients without voice complaints were compared prospectively with the 338 patients with dysphonia.

- **Methods**
- General Ear-Nose-Throat-objectives
- Videostroboscopy + voice analysis (SPEAD).
- Reading of a standard text in Danish ("The North Wind and the Sun"), and an intonation of a sustained tone /ah/ for the duration of four seconds in the lower register of the voice.
- The parameters for analysis of the videostroboscopic films; the shape of the arytenoids (**figure 1**) (+/-benign pathology of the vocal cords), especially focusing on oedema and redness.

Figure 1. The level of abnormality was here graded according to a 1-5 visual score, score 1 normal and 2-5 abnormality larynx as used in the clinic routinely, in which degree five is the maximum abnormal, and degree one represents normal arytenoids and vocal cords.

- The voice analysis of all with normal stroboscopy (score 1) or deviant parameters (score 2-5) included jitter% and shimmer%
- A closed quotient% of the electroglottogram was made, and standard deviations were made, using the SAS statistical system.

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Summery of results

Tables 1-2:

The pathological cases had significant higher measured values of jitter%, shimmer%, frequency and intensity.

- Qx% was measured with electroglottography. The pathological cases had lower values.
- When a differentiation was made between normal videostroboscopies (visual score of oedema including the arytenoids (1)) and abnormal ones (2-5), a difference for the closure time (Qx%) of the sustained tone /ah/ p<0,0001 is found (Welch ANOVA).
- The results suggested that with a standard deviation of Qx% less than 6,5 the voice is normal, and a standard deviation over 11,4-12,7 is pathological FOR sustained tone AND reading of a standard text in the lower register in non-professional voices.
- There was a statistically different result for all used parameters, between the 35 normal voices and the 338 pathological voices.

Table 3:

- Furthermore, 77 patients (ary 2-4) were analysed before and after updated medical treatment. There was not found any change for the jitter% and shimmer% with paired t-test.
- Qx% measurements with electroglottography showed a closure after treatment in sustained tones of + 4,6% (43,8 to 48,4%, p=0,0008).
- For the reading of the standard test, the regularity of frequency% was reduced (optimised) with 1,98% (p=0,053), the regularity of loudness% with 1,7% (p=0,004) and the Qx% had a change of 2,56% (p=0,044) analysed with paired t-tests (optimal Qx% = 50%).
- "A combined evaluation of the videostroboscopies and the voice analysis gives a better evaluation of the voice even if the shapes do not change much, the correlation between the standard text analysis and sustained tone taken into account".

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arytenoids shape 1-5		mean jitter%	Std Dev	mean shimmer%	Std Dev	mean Qx%	Std Dev	N	Comments
7A:	1	1,0	1,0	9,2	6,5	47,1	6,5	35	Wilcoxon test:
	2	3,4	8,1	7,6	5,3	45,6	14,8	70	common
	3	2,6	6,0	7,8	4,9	45,8	11,5	128	mean values
	4	5,6	15,4	8,7	7,5	44,6	13,0	129	for jitter% and
	5	4,5	7,2	11,8	16,6	47,9	7,9	11	shimmer%
statistics		-	-	-	-	significant difference between at least 2 groups for Qx% (p<0,05)			

B:

arytenoids shape 1-5		frequency variation%	Std Dev	loudness variation%	Std Dev	Qx%	Std Dev	N	Wilcoxon test:
	1	9,0	6,9	15,4	5,1	48,7	5,0	35	Equality
	2	13,2	11,9	16,8	6,8	44,7	13,8	70	cannot be rejected
	3	12,1	11,4	16,0	4,7	46,4	10,5	128	
	4	12,0	10,1	16,4	5,6	46,1	11,7	129	
	5	13,8	14,1	18,2	7,8	46,8	4,8	11	

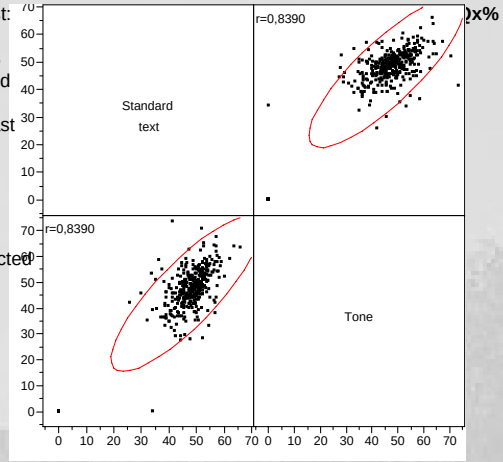

Table 1

A. Groups of consecutive digitized videostroboscopies evaluated by 2-3 observers on the spot, and voice analyses at the same time based on the pathology/oedema of the shape of the arytenoids in the larynx, grade 1=normal without laryngeal complaints, grade 5=maximal oedema and abnormality and **intonation of a sustained tone /ah/**. Comparison is made with jitter%, shimmer% and glottis closure time, Qx% measured with SPEAD by the firm Laryngograph ltd.

B.Discription of frequency, loudness and glottis closure variation by reading of a **standard text**: the North win and the sun at the same time on the same population.

Note the figure showing corcordance between reading af sustained tone measure

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A:

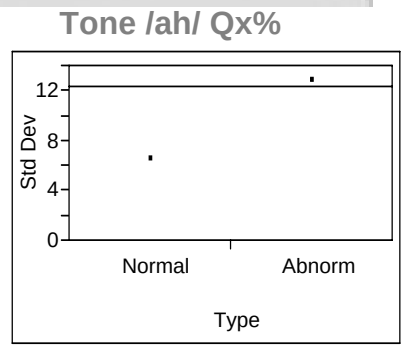
arytenoids shape 1	mean jitter%	Std Dev	mean shimmer%	Std Dev	mean Qx%	Std Dev	N
	1	1	9,2	6,5	47,1	6,5	35
shape 2-5	4	10,5	8,2	6,6	45,3	12,7	338
statistics	-	-	-	-	significant difference for Qx% and standard deviations between normal and abnormal measures, Welch ANOVA p<0,0001		

normals SD for frequency variation <6,9 abnormal> 11,1

arytenoids shape 1	frequency variation%	Std Dev	loudness variation%	Std Dev	Qx%	Std Dev	N
	9	6,9	15,4	5,1	48,7	6,5	35
shape 2-5	12,3	11,1	16,4	5,6	46,0	11,4	338
statistics	p 0,03 *		-		p 0,011 *		

normals SD for Qx% <6,5 abnormals >11.4

*p as given (Wilcoxon test)



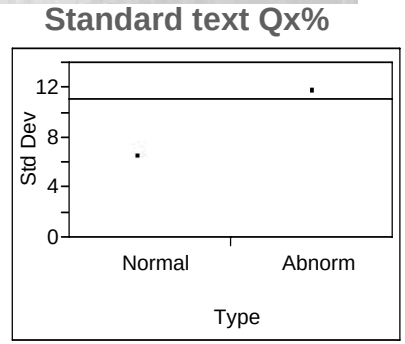


Table 2

Groups of consecutive digitized videostroboscopies evaluated by 2-3 observers on the spot, and voice analysis at the same time of normal controls: arytenoids shape grade1, without laryngeal complaints versus: abnormal clients with laryngeal complaints, arytenoids shape grade 2-5, measured with SPEAD by the firm Laryngograph ltd.**A**: **sustained tone /ah/. B**: reading of a **standard text:** the North wind and the sun.

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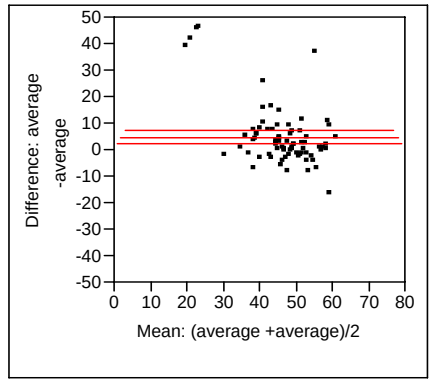
77 patients with examinations before and after medical treatment,
intonation of a sustained tone /ah/.

arytenoids abnormality	(shape 5 1 pt.)		(shape 5 3 ptt.)		
shape 4	1. examination	Std Dev	2. examination	Std Dev	N 1st 32/ 2nd.25
mean jitter%	5.7	17.9	1,1	1,1	
mean shimmer%	7,4	5,2	6,8	3,7	
mean Qx%	43,7	14,4	48,1	6,1	
shape 3	1.examination	Std Dev	2. examination	Std Dev	N 1st 26/ 2nd30
mean jitter%	3,8	8,7	1,6	3,0	
mean shimmer%	7,4	3,9	7,3	3,6	
mean Qx%	42,3	14,5	48,1	7,1	
shape 2	1.examination	Std Dev	2. examination	Std Dev	N 1st 16/ 2nd18

Table 3.

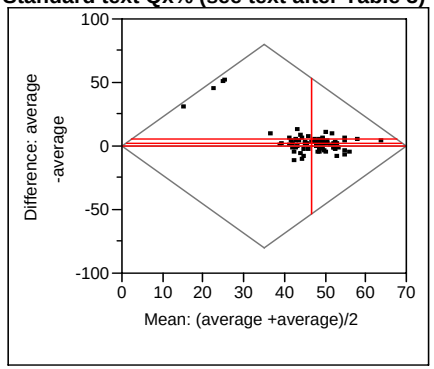
77 patients (groups of arytenoids score of deviation 2-5) were analysed before and after medical treatment. There was not found any change for the jitter% and shimmer% with Wilcoxon test. Qx% measurements with electroglottography showed a closure after treatment in sustained tones of + 4,6% (43,8 to 48,4%, p=0,0008). For the reading of the standard test, the regularity of frequency% was reduced (optimised) with 1,98% (p=0,053), the regularity of loudness% with 1,7% (p=0,004) and the Qx% had a change of 2,56% (p=0,044) analysed with Wilcpxon tests (optimal Qx% = 50%).

Tone /ah/ Qx% (Table 3)



average med 1 decimal 3

Standard text Qx% (see text after Table 3)



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Study 3

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Pedersen M, Munck, K (2007) A prospective case-control study of jitter%, shimmer% and Qx%, glottis closure, cohesion factor (Laryngograph Ltd.) and Long Time Average Spectra, Cost 2103, MAVEBA Italy: 61-64.

Aim and material was the same as study 2.

- Aim: to obtain "a statistical significant evidence of the videostroboscopic picture made in combination with voice analysis".

- **Materials**
- All patients coming in with complaints of a laryngeal disorder with hoarseness and a lump in the throat were analysed in a period of 4 months.
- 373 clients were included in this study, in which 35 of the patients were without voice complaints, and 338 patients were with dysphonia, diagnosed for medical disorders in the larynx and upper airways.
- The 35 consecutive clients without voice complaints were compared prospectively with the 338 patients with dysphonia.

- This study was made for "two still more advanced objective throat function analysis: the
- 1. Cohesion Factor of irregularity as defined in the Spead program by Laryngograph Ltd.
- 2. Long Time Averaging Spectrum (LTAS)" .

Methods

- By testing binary equal movements, related to the total amount of movement produces a Cohesion Factor of irregularity for Qx% and Fx% can be calculated **(Figure 1)** (for a sustained tone and a standard text). SPEAD.

- LTAS were recorded with SPEAD and analysed using the program Multi Dimension Voice Program (MDVP).

- **Figure 2a and b** show the LTAS of 338 pathological videostroboscopies and 335 normal ones

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Figure 1

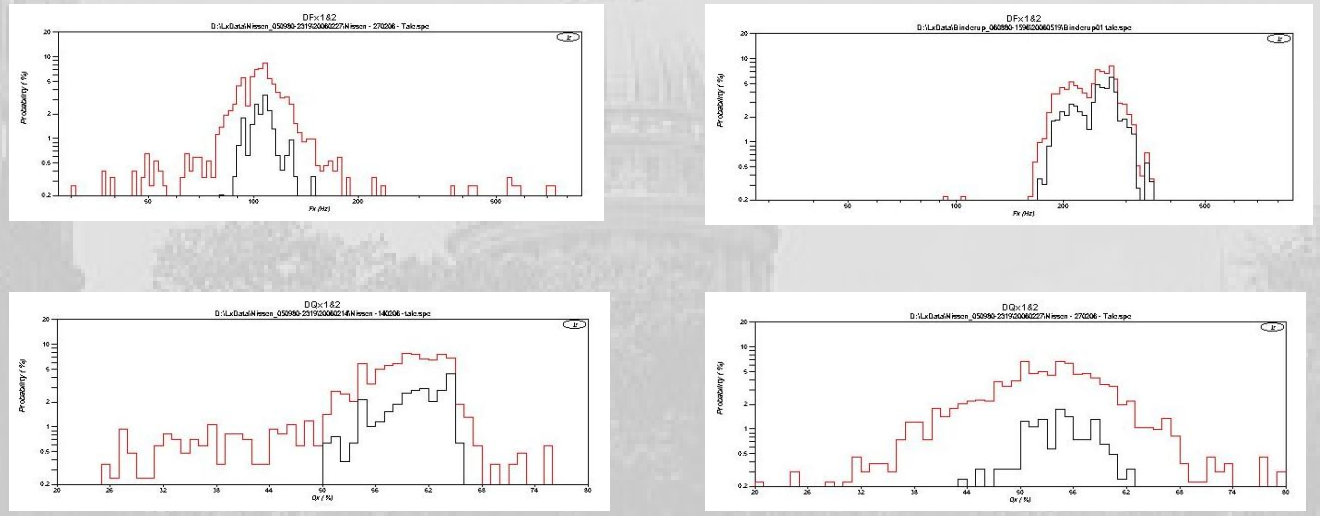

Figure 1.
Describes the cohesion factor, Fx%, also called the irregularity factor of the frequency before and after treatment and the cohesion factor of Qx% also called irregularity factor of the closed phase of the larynx. Both are the comparison of all measures, frequency measured with SPEAD and closed phases closed phases during reading of a standard text measured with electroglottography (SPEAD, Laryngograph ltd)**.**

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Figure 2

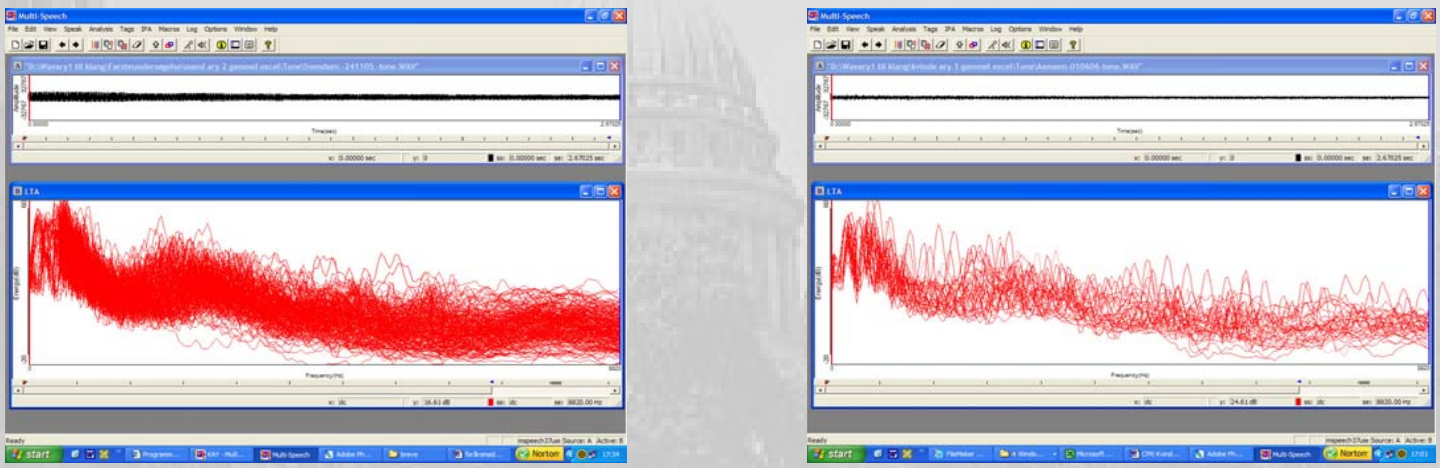

Fig. 2a shows the abnormals visual score 2-5 of the arytenoids oedema related to LTAS and **2b** the normal arytenoids visual score 1 related to LTAS

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- **Results**

- The analysis of 35 normals vs 338 abnormal larynx patients showed differences in cohesion factors (**tabel 1a + 1b**).

- In table 1b the cohesion factor changed for the closed phase of the electroglottogram in reading in a standard text from 44 to 37. 77 patients showed - after treatment - a change of the cohesion factor only for reading of a standard text measured of Qx% with electroglottography.

- In the LTAS, the area of 2500 to 4000 Hz had a different value comparing the normals with the pathological clients by reading of a standard text.
- **A significant** difference was found before and after treatment, illustrated in LTAS Product-Limit Survival Fit Survival Plot (for arytenoids oedema score 2-4)

	Sustained tone Qx%	**Reading of a text Qx%**
Arytenoid 1	19 (12-26) range	35 (30-40) **p 0,042*
Arytenoids 2-5	18 (15-20) range	41 (39-42) *difference*
	Sustained tone Fx%	**Reading of a text Fx%**
Arytenoids 1	1,9 (1-6) range	13 (8-19) **p ,03*
Arytenoids 2-5	5,3 (3,7-5,8) range	19(18-21) *difference*

Table 1a Cohesion factors for Qx% and Fx%, comparing normals with pathological clients

	Sustained tone Qx%	**Reading of a text Qx%**
before	17 (12-22) range	44 (40-48) *p*0,015*
after	14 (9-19) range	37 (33-41) *difference*
	Sustained tone Fx%	**Reading of a text Fx%**
before	4.5 (1.8-7.2)	22 (19-26)
after	3 (0.3-5.7)	17 (14-22)

Cohesion factor before and after treatment arytenoids score 2-4

Table 1b comparing clients before and after treatment

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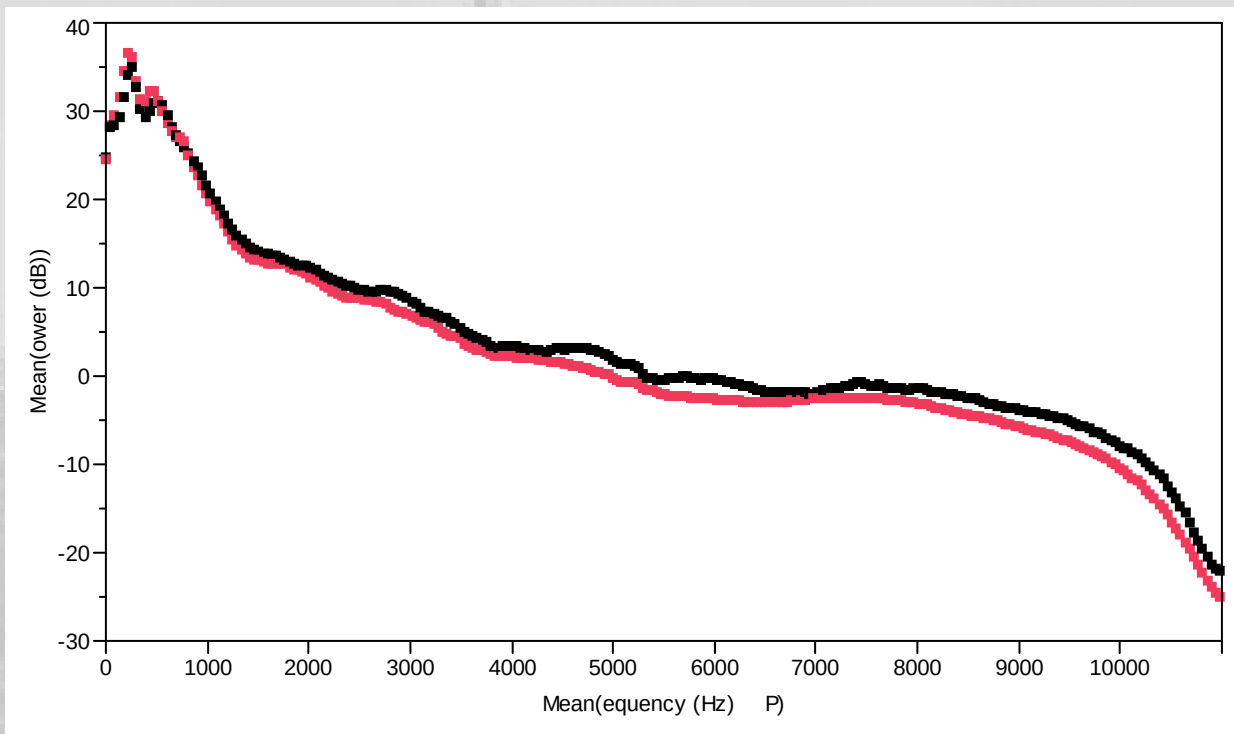
LTAS in normals with arytenoids score 1 vs. abnormals with arytenoids score 2-5

Overlay Plot for 0 – 10.000 1 vs 2-5 in reading of a standard text



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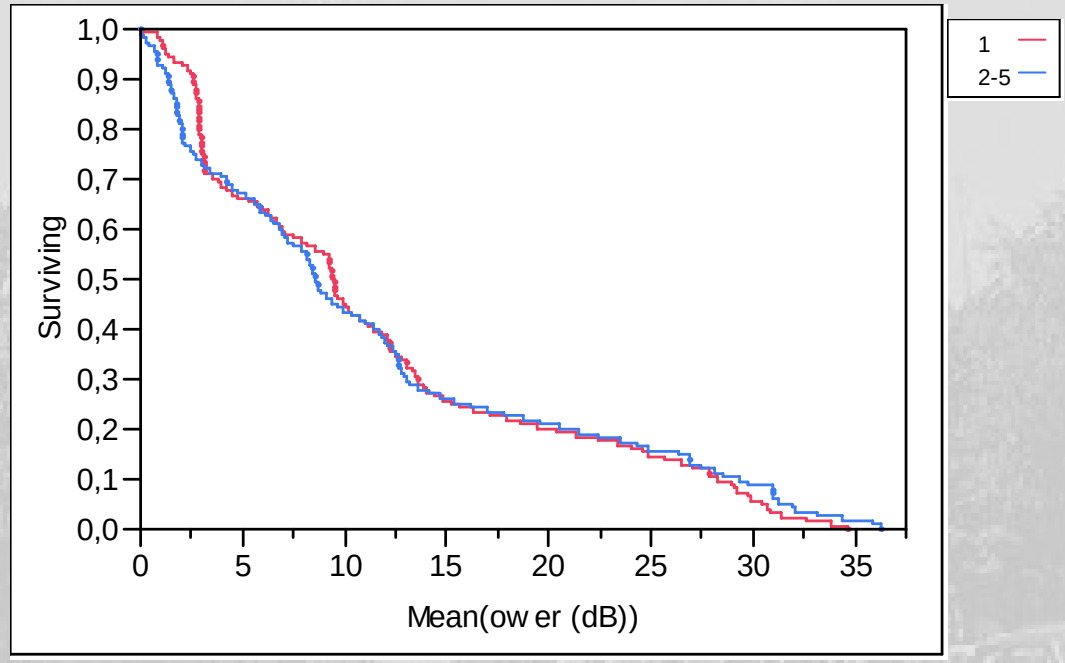
LTAS in normals with arytenoids score 1 vs. abnormals with arytenoids score 2-5

Product-Limit Survival Fit
Survival Plot for 0 - 10.000 1 vs 2-5 in reading of a standard text



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LTAS in normals with arytenoids score 1 vs. abnormals with arytenoids score 2-5

Summary

Group	Number failed	Number censored	Mean	Std Error
1	124	0	11,5904	0,84845
2-5	115	0	11,5183	0,94524
Combined	239	0	11,5557	0,63163

Quantiles

Group	Median Time	Lower95%	Upper95%	25% Failures	75% Failures
1	9,4464	7,0491	11,004	3,0921	15,667
2-5	8,6174	6,9398	11,015	2,6282	16,169
Combined	9,2939	7,9248	10,166	2,966	15,667

Tests Between Groups

Test	ChiSquare	DF	Prob>ChiSq
Log-Rank	0,0723	1	0,7879
Wilcoxon	0,4110	1	0,5214

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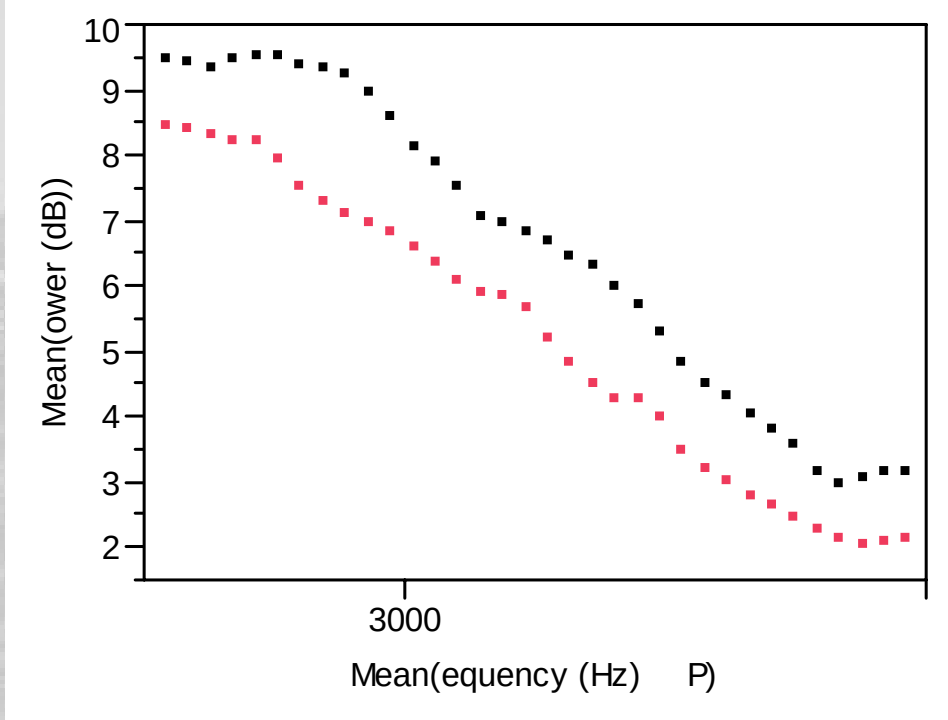
LTAS in normals with arytenoids score 1 vs. abnormals with arytenoids score 2-5

Overlay Plot of 2500-4000 1 vs 2-5 in reading of a standard text



1 = black

2-5 = red

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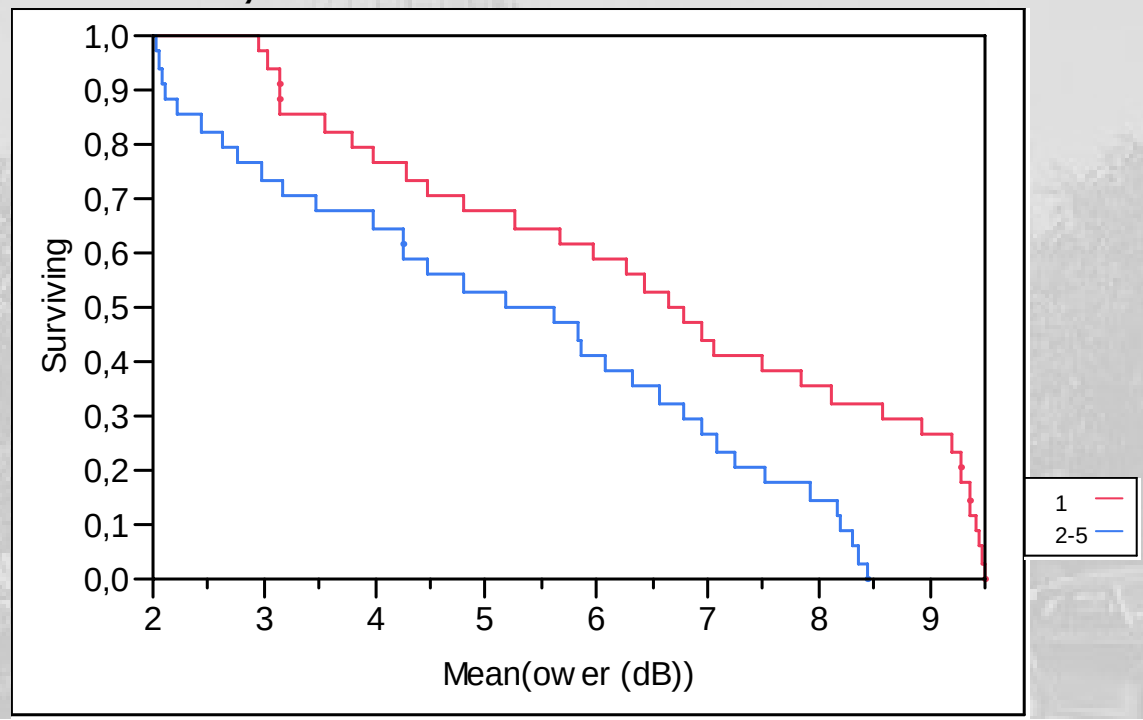
LTAS in normals with arytenoids score 1 vs. abnormals with arytenoids score 2-5

Product-Limit Survival Fit Survival Plot for the area of 2500-4000 Hz in the groups 1 vs 2-5 in reading of a standard text. Both the Log-Rank and Wilcoxon showed significance difference with the scores 0,0025 and 0,0153



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LTAS in normals with arytenoids score 1 vs. abnormals with arytenoids score 2-5

Summary

Group	Number failed	Number censored	Mean	Std Error
1	34	0	6,54782	0,40702
2-5	34	0	5,17811	0,38149
Combined	68	0	5,86296	0,2892

Quantiles

Group	Median Time	Lower95%	Upper95%	25% Failures	75% Failures
1	6,647	4,7858	8,1139	4,2727	9,1948
2-5	5,1709	3,4625	6,5781	2,966	7,085
Combined	5,9712	4,7858	6,7882	3,7927	7,9248

Tests Between Groups

Test	ChiSquare	DF	Prob>ChiSq
Log-Rank	9,1651	1	0,0025
Wilcoxon	5,8763	1	0,0153

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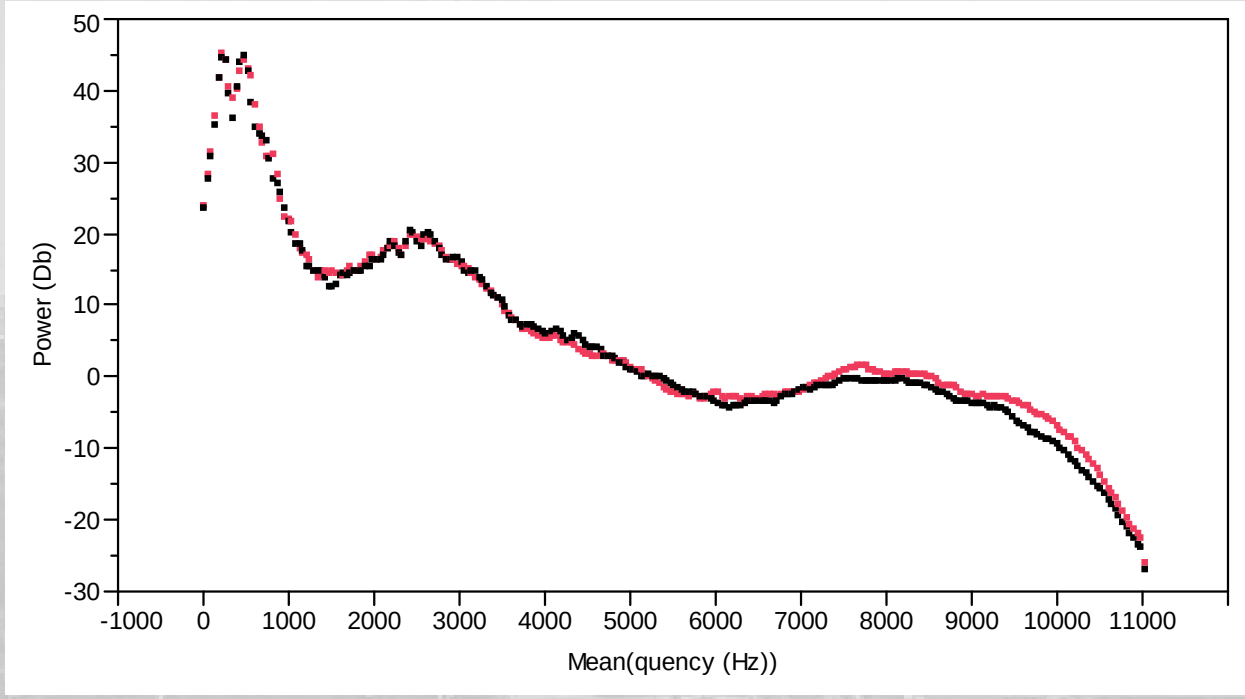
LTAS Product-Limit Survival Fit Survival Plot group 2-4 before and after treatment showed a significance difference in Wilcoxon (Prob>ChiSq) between the two groups (0,0207).

Overlay Plot group 2-4 before and after treatment



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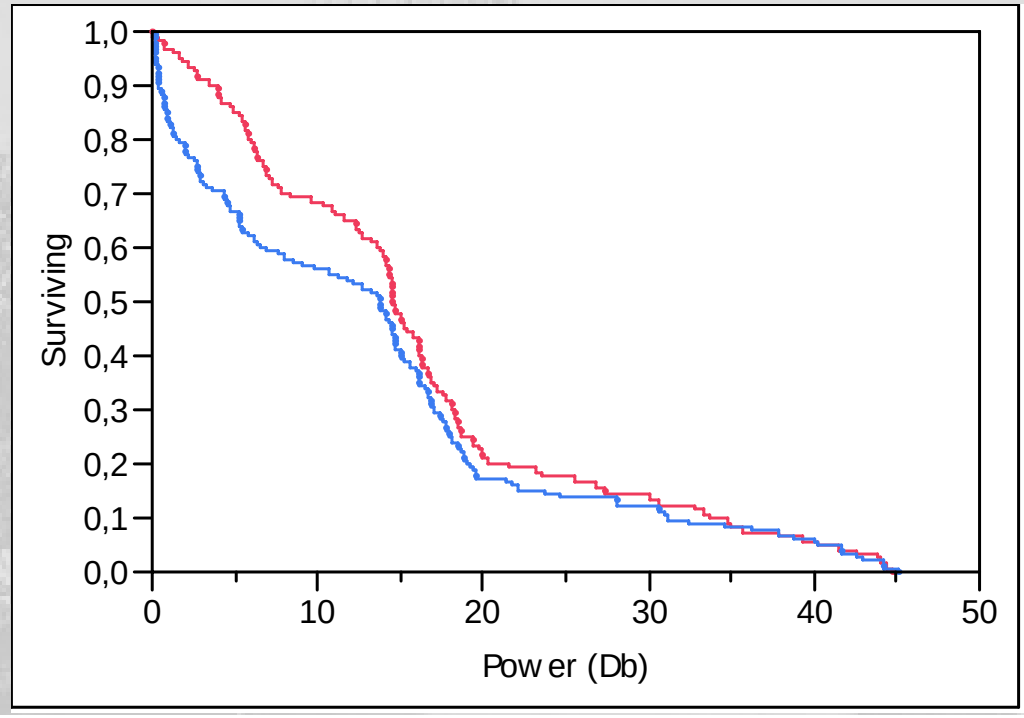
LTAS Product-Limit Survival Fit Survival Plot group 2-4 before and after treatment showed a significance difference in Wilcoxon (Prob>ChiSq) between the two groups (0,0207).

Product-Limit Survival Fit Survival Plot group 2-4 before and after treatment showed a significance difference in Wilcoxon (Prob>ChiSq) between the two groups when holding a sustained tone (/Ah/). Red after treatment



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LTAS Product-Limit Survival Fit Survival Plot group 2-4 before and after treatment showed a significance difference in Wilcoxon (Prob>ChiSq) between the two groups (0,0207).

Summary

Group	Number failed	Number censored	Mean	Std Error
Efter	120	0	15,9108	1,01067
Før	145	0	13,2967	0,99122
Combined	265	0	14,4804	0,71284

Quantiles

Group	Median Time	Lower95%	Upper95%	25% Failures	75% Failures
Efter	14,58	13,686	16,071	6,7983	19,413
Før	13,798	7,9709	14,674	2,7317	18,003
Combined	14,395	13,267	15,037	5,1688	18,525

Tests Between Groups

Test	ChiSquare	DF	Prob>ChiSq
Log-Rank	1,6061	1	0,2050
Wilcoxon	5,3489	1	0,0207

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Discussion

- The design of the first reviewed study was based on the historic lack of evidence concerning voice therapy for non organic voice disorders.
- These were in a prospective blinded study compared with the new knowledge of medical disorders caused by allergy, infections, reflux and environmental irritants distorting the microwaves of the vocal folds, which move up to many hundreds per second.
- These kinds of systematic diagnoses and treatments should be made “routinely by laryngologists treating dysphonic patients when the stroboscopy reveals no other pathology than movement: change of amplitude, mucosal wave, irregular fluctuation of the vocal folds or insufficient closure and eventual slight deviations of the form of the vocal cords

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Discussion

- In study two, a better definition of normality was shown, comparing videostroboscopy including oedema especially of the arytenoids with the voice parameters of jitter shimmer, and Qx% of the vocal cords (closure time as measured with electro-glottography).
- No other evidence based studies exist.
- It was also shown that jitter% and especially Qx% of vocal cords are related to medical treatment of pathological changes of the larynx (including the arytenoids).

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Discussion

- In study three the cohesion factor was reduced in tone and text after treatment. The LTAS measurements showed that the area of 2500 to 4000 Hz had a higher value in dB for the normal group than for the pathological group. The treatment effect in the pathological group showed a better LTAS after treatment while reading the standard text.

- These studies have hereby provided us with prospective case-control and cohort studies of measurements for the future treatment of laryngeal voice disorders.

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Further discussion

- We have found that the clinical documentation with physiological and acoustical parameters - of treatment, related to mediators of inflammation and mucosal treatment of the upper airways can be made in the larynx.
- A great deal of research on inflammation mediators has been made in the area of the nose and the ears. The throat has probably been too complicated to many researchers due to the combined respiration-, swallowing- and voice- aspects. Researchers should keep in mind in their research protocols for upper airways studies that throat analysis is involved when nose and ear mediators of inflammation are looked upon.
- This means that a minimal knowledge of voice, laryngeal - respiration aspects and swallowing is necessary in the future for anybody studying upper airways mucosa.

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Further discussion

Taking into account that the most frequent disorders in the lower part of the upper airways: vocal nodules and laryngo-pharyngeal reflux have no evidence based reference, research protocols of inflammation mediators for randomised controlled studies should include measurement of reflux, voice, and respiration aspects, macroscopically and microscopically tissue research.

Another aspect is the new possibility for genetic tests e.g. of lactose enzymes in milk. In a prospective clinical study of 314 patients with hoarseness during 6 months in the year 2007, 12% had lactose milk intolerance. Once the lack of results of evidence in earlier studies are accepted, not only focus on new kinds of diagnoses but also of treatment of inflammatory disorders of the upper airways must be made. To rely alone on nose or ear function without taking the throat function into account is questionable. Referring to “functional voice disorders” is scientifically not better than “functional” nose or ear disorders.

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Conclusion

The understanding of measurement of for example genes, steroid and neurone receptors, bacteria, primary and secondary immunological defects and environmental toxins in the larynx **is necessary for protocols for randomised controlled studies of inflammation mediators of the upper airways including the larynx.**

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